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PEDIATRIC ANESTHESIA

Special Report No. 179

Charles E. Fierst, M.D.*

Anesthesia for pediatric surgery is the application of all known modern techniques of anesthesia modified to comply with the demands of a pediatric physiology. Not only is a knowledge of the agent or technique essential, but it is imperative that the physician have a knowledge of the physiology of the two basic systems involved, namely, the respiratory and circulatory systems of the infant.

The average respiratory rate of a newborn is about 40 per minute, but this may vary from 20 to 100 per minute. There is synchronous protrusion of the chest and diaphragm indicating intercostal and diaphragmatic action, frequently the diaphragmatic predominating. Irregularity of respiration and periodicity occurs frequently during the first few weeks of life. The tidal air of normal respiration of the newborn is approximately 15–20 milliliters but may be increased to 180 milliliters by crying or other respiratory activity. One-third of this tidal air represents dead space air. It is obvious that interference with normal tidal air by anesthesia or obstruction for a relatively short period of time can be tragic in its consequences. Real obstructions to respiration curtailing the oxygen supply are seen with glottic spasm, enlarged tonsils and adenoids, valve-like action of tongue sticking to the hard palate, or excessive secretions. Respiration is arduous under these conditions, with the diphragmatic activity predominating, and may be associated with phonation. This phonation is usually inspiratory in phase, the cords adducting during inspiration.

Occasionally the respiration is reversed and the inspiratory pause prolonged. It may consist of several short inspiratory efforts followed by a regular full expiration. This type of breathing is not injurious, in fact the oxygen intake is above normal, but it can be very disconcerting to the surgeon. This is commonly described as a sobbing respiration, and at times thwarted every attempt to overcome it, until the appearance of curare in the anesthetic horizon.

It may be well to mention at this time, a condition peculiar to infants. During the inspiratory phase of respiration a negative pressure is produced in the stomach, and the infant is capable of ingesting large amounts of air or oxygen. This ingestion is greatest when respiration becomes obstructed, either by irritating vapors, collection of mucus, or trauma under light

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anesthesia. Only .4 millimeters mercury pressure is necessary to overcome the negative intrapleural pressure, so over-enthusiastic efforts at resuscitation or positive pressure will definitely contribute to this condition, and give the appearance of a profound respiratory depression, grunting respiration, cyanosis, and marked distension of the abdomen with bulging in the upper left quadrant. This condition can so closely resemble the symptoms of an acute ruptured viscus as to lead to surgery. The symptoms may be transient or persist indefinitely unless treated. The passage of a soft rubber catheter into the stomach will relieve the distress immediately.

Under general anesthesia, many variations of the respiratory rate may occur. The rate of an infant may reach 120 per minute from acidosis, hypoxia, or reflex stimulation from the anesthetic agent or surgical procedures.

Gaseous acidosis from faulty carbon dioxide elimination should be relieved by reduction in the dead space. Even the smallest anesthetic mask will double the dead space unless a high flow of gases are maintained to wash away the expired carbon dioxide. Also reduction of the dead space is accomplished by removing mask covers or towels, use of a Leach gasway, efficient carbon dioxide absorption, or endotracheal technique. Non-gaseous acidosis, common in ether anesthesia, can be combatted by intravenous or rectal fluids.

Intubation with an endotracheal catheter decreases both the mechanical and physiological dead space; the physiological dead space is estimated at 150 milliliters, while the mechanical dead space has been estimated at 200 milliliters. With an endotracheal tube in place, it is estimated that the cubic space is only 14 milliliters and as most of the gas is channeled through the tube, it is obvious how much of the dead space is removed.

Hypoxia may stimulate chemically through the carotid and aortic bodies. When it becomes severe, depression of respiration occurs, and the vital factor is oxygen supply. The average adult oxygen consumption is about 3.9 milligrams per kilogram of body weight per minute; in the newborn, 7 milliliters per kilogram of body weight per minute is required. Thus, newborns weighing from 3 to 5 kilograms will require 21 to 35 milligrams of oxygen per minute. From one to three years of age the child consumes even more oxygen, in proportion to its weight, than does either the newborn or the adult. The criteria of oxygen demand in hypoxia are still the physiological ones of rapid, irregular respirations, slow pulse, pallor, cyanosis, and muscular contractions; but these at times are not too sensitive.

Difficulties in pediatric anesthesia usually involve the respiratory system which can be tolerated for several minutes, but cessation of circulation, with its fatal anoxia, is complete in a matter of a few seconds. The circulation of an infant is very variable but less susceptible to circulatory acci-

dents, and in these respects differs from the adult. For example, the heart rate of an infant under ether anesthesia may be from 200 to 180 per minute; with sudden breath holding, it drops to 100 to 60 per minute. The heart rate is also susceptible to sudden thermal changes. Sinus arrhythmias are occasionally seen in adults but are frequently encountered in infants and children. Pathologically of no significance these can be controlled temporarily by the administration of atropine sulphate. The average normal heart rate is 180 per minute at birth and 120 per minute at one year, the greatest variable being after the first twenty-four hours of life, with an approximate rate of 135 per minute.

At birth the blood pressure is approximately 75/39 to 85/40. During the first fourteen days, it rises to around 20 millimeters of mercury, but from this time on, it only rises an additional 5 millimeters by the end of the first year. Dehydration and severe crying will raise these values. On the whole, blood pressure records are not so valuable during the first year of life as they are later, but increased divergence in the ratio of an increased pulse and falling blood pressure is significant of a failing circulation and impending shock.

From the works of Lucas-Dearing and Robinow-Hamilton, it can be assumed that there are approximately 100 milliliters of blood for every kilogram of body weight. Therefore, the old practice of giving 10 milliliters of fluids or blood per pound of body weight has a glaring discrepancy and is not physiologically sound. One should attempt to approximate the loss or deficiency, and restore the volume on known criterion.

The minute volume of blood of an infant is approximately twice that of an adult, being roughly 520 milliliters per minute or 4 to 5 milliliters per beat. The circulation time is around 12 to 14 seconds, also faster than the adult; both are beneficial in emergency cases with low hemoglobin values.

The hemoglobin content of the blood of a normal newborn is usually around 18 grams per 100 milliliters of blood. This value decreases rapidly during the first two weeks of life, and the blood cells become smaller at the same time. At the end of the first year the hemoglobin is usually around 12.5 grams per 100 milliliters and gradually increases to 15 grams per 100 milliliters of blood in adulthood.

Electrocardiography on anesthetized infants under three months of age will quite often have extrasystoles, absent T waves and right ventricular preponderance. Clinically these are taken as a normal observation.

Armed with a few of the pertinent facts of infant and child physiology we approach the problems of anesthesia with a greater degree of certainty.

The adventure of walking into the unknown is just as awesome, stimulating, and fear-producing for the little people as the adult. These normal reactions can be accentuated or partially allayed by the first thing you do

—your approach to the patient. The average child from an average normal home will respond to a kindly, understanding, pleasant expression on the face, discussion of toys, games and desirable physical attributes, and an honest description of the procedures necessary to reinstate him or her to good health. Of course, there are those little darlings of neurotic, nervous parents that will throw your office, clinic, or operating room into pandemonium. It has been my experience that firm but gentle handling, directness of purpose, and as little conversation as possible will pacify the nervous and maligned patient. Then too, we have another ally at our command—the drugs of premedication. However, in order to use these drugs judiciously, one must know something of the general physical condition of the patient. To violate the principles of good medicine and anesthesia will produce a far graver condition than the original condition to be corrected.

A reasonable history and physical examination provides important information:

1. History of difficult labor or forceps delivery may have been injurious to the patient's brain, either from anoxia or intracranial hemorrhage.
2. Story of convulsions warns one to order or give adequate barbiturates.
3. Retarded development with late or abnormal responses, such as inability to raise the head, to grasp objects, to sit up, or to stand. These are clues to the muscular system or mental retardation.
4. History of severe attacks of scarlet fever, diphtheria, rheumatic fever, nephritis, or chronic suppurative conditions warns that the heart, kidney and liver may have impaired functions.
5. History of prolonged bleeding or unreasonable ecchymosis to a minor trauma suggests a blood dyscrasia.
6. Frequently, attacks of pneumonia suggest the presence of an underlying bronchiectasis or atelectasis with an increased risk of post-operative pulmonary complications.
7. Recent meal or feeding and time relation to trauma. This is important because the normal emptying time of the stomach can be delayed from one to three hours by the proximity of the ingestion of food to the time of the trauma or severe pain.
8. Copious vomiting rapidly produces severe acidosis and dehydration in infants and young children.

Physical Examination:

1. Pale, asthenic children with little subcutaneous fat and transparent skin do not withstand anesthesia or surgical abuse.
2. Jaundice, cyanosis, and edema add to the risk of anesthesia, and their underlying causes should be appreciated.
3. Presence of numerous bruises often indicates a blood dyscrasia with a prolonged bleeding time which excludes anesthetic procedures such as a nasal intubation which may produce trauma and bleeding.
4. Adenoid facies, crusting around the nose, ankylosis of the jaw, deformed bony thorax, predominance of diaphragmatic breathing must not be overlooked.
5. Inelasticity of the skin, dry tongue, sunken eyes, and depressed fontanelles are signs of dehydration. This must be corrected with fluids before operation.

6. Foreign bodies in the mouth may be bizzare in character from chewing gum to nuts and bolts.
7. Arrhythmias, pathological heart murmurs, and blood pressure should be noted and evaluated.
8. Determination of "apparent age" is far more important than the real age in prescribing dosage of premedication.

Laboratory Tests:

1. Extremely low levels of hemoglobin are encountered in cases of nutritional anemia. Readings as low as 5 grams per 100 millileters are encountered. These values should be known for the varying degrees of cyanosis to be interpreted correctly. The infant with 18 grams hemoglobin per 100 milliliters of blood can easily have 5 grams of reduced hemoglobin, can exhibit cyanosis, and can still have adequate oxyhemoblobin. The anemic child with 5 to 6 grams of hemoglobin will slow a pale cyanosis only when he is in a state of severe hypoxia. However, a low value does not necessarily contra-indicate the use of anesthesia in emergencies in infants, because the rapid circulation time (12 to 14 seconds) plus proper oxygenation helps to overcome this deficiency of oxygen-carrying hemoglobin.
2. Urine of high specific gravity is often a sign of dehydration.
3. Acetonuria is seen in many children and can be overcome with intravenous, subcutaneous, or rectal electrolytes or fluids.
4. Albuminuria suggests kidney damage, but must be distinguished from orthostatic albuminuria.
5. Glycosuria is rare, and may denote a diabetic condition.
6. Bleeding and coagulation time is done more or less routinely, but has more of a medico-legal value than real insight to the clotting ability of the individual's blood.
7. Positive tuberculin tests should be followed by x-ray of the chest before the type of anesthetic agent is determined. Positive x-ray findings may contra-indicate agents that are irritating to the lungs, and the case can be accomplished under spinal block anesthesia.

The proper pre-anesthetic care and premedication of the infant or child is the index to good anesthesia, successful surgery, and a smooth convalescence. The procedures of good preanesthetic care are these:

1. A clear and friendly environment.
2. Relief of pain by oral aspirin (grains 1 to 5), by hypodermic codine (1/8 grain to 1 grain), morphine sulphate (grain 1/480 to 1/8), or by demerol (13 milligrams to 75 milligrams) as determined by apparent age.
3. The attenuation and therapeutic treatment of convulsions by barbiturates. These may be administered rectally, intravenously, or orally. The drugs of choice are avertin, pentobarbital, and phenobarbital. The oral drugs may be mixed with corn syrup to conceal the bitter taste and also to supply glucose.
4. Restoration of body fluids and blood volume components by intravenous, subcutaneous, and rectal administration of electrolytes; the intravenous use of plasma and whole blood.
5. Toilet of the lower intestinal tract by enema which prevents evacuation on the table and post-operative rise in body temperature.

6. Withholding of food:
   A. In infants who are fed every four hours, if the operation is in the early morning, the midnight feeding is given. If operation is in the late morning, the 4:00 A. M. feeding is allowed. Water may be given up to an hour before anesthesia.
   B. In older children breakfast is withheld for morning operations. If the case is to be done in the late afternoon, a non-residue breakfast is permitted.
7. Routine procedures of preparation are not always possible for there are those emergency cases which can confront one with bizarre problems. This usually occurs in healthy children with a full stomach, and it must be remembered that the digestive processes practically cease following severe trauma, thus retarding the emptying time of the stomach from one to three hours. It is my opinion that gas anesthesia should be avoided at all costs, even that malignant "little whiff" that is so frequently asked for. Spinal, block, intravenous nembutal—morphine, local, avertin, and local techniques substituted. If it is unavoidable to use a gas-technique, the patient should be placed in Trendelenburg position with suction ready and induction with nitrous oxide. The addition of ether to the mixture is usually enough to cause retching and vomiting. After the vomiting and toilet of the pharynx with suction, the anesthesia can be deepened to any level necessary. It is obvious that it leaves much to be desired in the anesthetization of emergency cases for lavage is a very trying and exhausting experience for an excited and apprehensive child, and only partially successful in cleansing the stomach in my experience. An attempt to intubate under anesthesia usually precipitates vomiting, even with rapid induction and passing of an endotracheal catheter in patients whose stomachs have or have not been lavaged. The best advice at this time is to avoid inhalation anesthesia if possible; if not, great care should be taken and the anesthetist must be on the alert for any crisis.

Having knowledge of the patient's present physical condition along with a general knowledge of the past history and the apparent age, one is prepared to premedicate the patient. Let me make it clear that the patient is not made to fit a routine table of premedication; there should not be any routine table, but premedication is made to fit an individual case, kind of anesthetic, and type of surgery.

The three groups of drugs generally used for premedication are the opiates, barbituarates, and belladonna derivatives. They may be given alone or in combinations; orally, subcutaneously, intravenously or rectally.

Practically every drug listed in the phamacopoea has, in addition to the beneficial effects, annoying or deleterious side effects. This is true of the drugs just mentioned for premedication, but in the judicious use of these agents for individual cases and techniques, the advantages outweigh the disadvantages in my estimation. In those cases requiring my absence from the operative field, in which an ether hook, Waters airway, or endotracheal catheter is required, I particularly like to use the belladonna derivatives or atropine sulfate in patients under five years of age and scopolamine in children over five years of age. Excessive mucus secretions under these circumstances can be very trying to the anesthetist and deleterious to the patient. Also, the belladonna drugs may inhibit or prevent, in adequate dosage, the vagal reflexes, and carotid sinus reflexes which might occur under barbiturate or light anesthesia.

In pediatric premedication, opiates have a very definite place in children of an apparent age of five years or older, where drop ether is not the anesthetic

agent. In excessive doses, both drugs depress the respiratory center. For surgery of the thorax to the toes, where gas-oxygen, with or without curare, spinal or block anesthesia are to be used, the opiates produce a basal narcosis, which lessens the amount of anesthetic agent required and raises the pain threshhold. The use of intravenous morphine in children is not only applicable, but most desirable in certain situations, as in unprepared emergency cases, diminishing anesthesia in spinal or block techniques, and in severely burned patients. The real danger of morphine in my mind is the extrinsic factor of the personnel preparing the dosage, rather than the intrinsic pharmacologic action. The only undesirable reactions to intravenous morphine, in my experience in children and adults, has been due to too rapid administration.

The barbiturates are a welcomed addition to our armamentarium of premedication. The short acting drugs as, nembutal or seconal, are the more popular ones. When used in combination with the opiate-belladonna drugs they make their presence felt by increasing sedation, lowering metabolic rate, lessening the incidence of convulsions and helping to prevent shock. However, when prescribed along in the presence of pain, they may produce excessive secretions and uncontrollable excitement.

It is difficult to disassociate the basal anesthetic drugs, avertin and rectal sodium pentothal, evipal, seconal, and paraldehyde from the agents of premedication. Fundamentally that is all they are and I never use them as the anesthetic agent in combination with morphine in children, severe liver damage, acute inflammatory diseases of the lungs or lower bowel and severely burned patients. However, for the nervous and apprehensive child or youngsters requiring multiple operations, in proper dosage it is particularly suited to them. On two points I will be dogmatic, first, the dosage of avertin in young children in generally good health, is 100 milligrams per kilogram of body weight because of their rapid detoxification and high metabolic rate; anything less and you have wasted the drug and your time, secondly, it is contra-indicated in surgery of the mouth or throat unless endotracheal technique can be used. The child is asleep in approximately eight minutes after avertin has been administered and the average recovery time is one hour and fifteen minutes. The real danger of the basal anesthetics is due to improper or negligent nursing care in maintaining a proper airway immediately after the administration of the drug and return of the patient to the room after surgery. Of the other drugs used rectally, avertin is the most consistent in action and dependability in my experience.

Time does not permit a detailed description of the various anesthetic agents or techniques of administration. The best approach to this discussion is by age groups.

From birth to three years of age, open drop ether is best from the standpoint of potency and safety. Mask administration conforms more closely to physiologic gaseous exchange, for the agent is delivered with a minimum of effort to the lungs. In cases of brain or thoracic surgery, where position and positive pressure are essential, endotracheal technique can and should be used. Great care should be exercised at intubation of these infants for the smaller rima of the larynx, the more apt it is for resulting edema to cause obstruction and asphyxia. In disagreement with some authors, I never use curare in conjunction with straight ether anesthesia, for they simulate and intensify each other's action in this age group. For rapid induction of these infants, ethylchloride or Divenyl-ether (vinethene) may be used, but with one important precaution, be certain the air or oxygen intake is sufficient. The usual premedication of

this group is limited to the belladonna group, especially when intubation is anticipated or when a technique is used which will permit the anesthetist to be away from the operative field. Barbiturates are also used in extremely restless infants or in those known to have convulsive seizures.

From the apparent age of four to twelve years all the modern anesthesia techniques and agents are used safely and successfully. However, the use of intravenous sodium pentothal is limited to those children of the apparent age of ten years or older as the anesthetic agent. It may be used in younger children as a supplemental agent in 1 to 2½ per cent solution.

The introduction of curare into the anesthetic field has been a boon to pediatric anesthesiology.

I prefer d-tubocurarine chloride because of its more constant and longer action in a dosage of 2 minims (0.12 milliliters) per 5 pounds or 2 kilograms of body weight. With this dosage it is now possible to use the gas-oxygen agents with satisfactory skeletal muscle relaxation without employing heavy premedication or deep basal sedation. Less anesthetic drug is required, therefore, the normal physiology is little disturbed; the normal reflexes are regained promptly following surgery; and the post-anesthetic complications are practically nil. My preferred combination is cyclopropane, oxygen, and curare; and I only deviate from that choice when severe congenital or pathological heart lesions exist or when electrical or x-ray equipment is to be used during the operation. Occasionally, an arrythmia will develop from too heavy a concentration of cyclopropane and all that is required for correction is the discontinuation of its use for a time, then its reinstatement in a more diluted mixture. However, if the arrythmia should persist, curare having been given, it is quite simple to use the other gases or gas-ether. Also epinephrine should never be used or given while cyclopropane is the agent for it may produce ventricular fibrillation. The more recent synthetic curare-like preparations: syncurine and netubine, are now being used clinically. Syncurine is quicker acting and more potent but it has a shorter action time. It is particularly applicable in fortifying waning relaxation in long cases when the surgeon is ready to close the abdomen. Its action is immediate and it has a rapid detoxification time of about 15 minutes. It has less tendency to produce bronchospasm than intocostrin or d-tubocurarine. The dose of syncurine is minim 1 (.0600 milliliters) per 5 pounds or 2 kilograms of body weight. One must always be prepared to take control of the breathing by manual compression of the reservoir bag if and when respiratory depression occurs from paralysis of the intercostal and respiratory musculature.

Spinal anesthesia has been a great aid in cases where other agents might produce untoward results. The dosage of 1 milligram of procaine hydrochloride per pound of body weight has been safe and adequate in my experience. In cases of intestinal obstruction, diabetes, and cardiac decompensation it has worked well with the usual constant vigilance of respiratory rate, blood pressure, and pulse rate. Pre-spinal vasopressors are not used in the small children because the sympathetic nervous system of these patients is extremely sensitive to them. However in older and larger children 1/6 the adult dose of vasopressors may be given as a subcutaneous pre-anesthetic. The drugs I most commonly use in older children are ephedrine or methedrine. Patients having spinal anesthesia should receive the maximum dosage of premedication for their apparent age and physical condition because they become very restless and do not tolerate well the unfamiliar numb feeling of their lower appendages. Some-

times analgesia with nitrous oxide, intravenous nembutal, or morphine have to be used to quiet the small patient.

Local anesthesia (regional and field blocks), is applicable in pediatric as well as adult surgery with modifications. In very small infants, not only the concentration of the drug but also the amount of the drug has to be reduced. Procaine can be diluted to .25 to .50 per cent and the total amount must be reduced to less than half of the average adult dose. Also, analgesia must be supplied for the younger children become very restless and irritable under local anesthesia. I prefer not to use vaso-constrictors with it in infants and small children, for areas of necrosis may occur at the site of injection and there is a possibility of marked reaction of their sympathetic nervous system to this class of drugs. In older children it is not necessary to lessen the concentration but it is important to cut down the total dosage.

The general complications of local anesthesia are syncope and convulsions. The syncope can be controlled by position, stimulants, and oxygen. The convulsions can be treated with oxygen, cyclopropane anesthesia, and intravenous barbiturates of nembutal or sodium pentothal. Care must be exercised not to overdose the patient with barbiturates, nor should a profound respiratory depression be added to the existing condition.

SUMMARY

In closing I would like to summarize the pertinent points of pediatric anesthesia:

1. Anesthesia for pediatric surgery is the application of all known modern techniques modified to comply with the demands of a pediatric physiology.
2. The criterion of dosage of drugs should be based upon the apparent age and physical condition of the patient.
3. Anatomical differences inhibit the use of certain drugs and anesthetic equipment at times.
4. The great advantage of intubation is the elimination of dead space and the judicious use of positive pressure.
5. Curare is a tremendous help in producing good surgical anesthesia by limiting the use of drugs and techniques which might produce changes in hydrogen-ion concentration and/or severe anoxemia.
6. The discriminate use of fluids and blood in anesthesia should be emphasized.
7. Psychic trauma is minimized by the art of induction.

AUREOMYCIN IN THE TREATMENT OF PERITONITIS OF APPENDICEAL ORIGIN*

Bennett Olshaker, M.D.
Joseph M. LoPresti, M.D.
Richard L. Jackson, M.D.

Peritonitis secondary to ruptured appendix has long been an important problem in the pediatric age group. The diagnosis of appendicitis in infants and children is a difficult one, and often perforation has occurred before the diagnosis is established.

Ladd and Gross[1] report a mortality of 6.9 per cent in a series of 405 cases of acute ruptured appendicitis with local or diffuse peritonitis. These patients were treated during the years 1928–1939. Others[2] indicate that the mortality varied from 10 per cent to 20 per cent. These reports, however, are from the era before the use of chemotherapy. Since the advent of sulfonamide drugs and the various antibiotics, the outlook is apparently not so grave. Altemeier[3] has reported a reduction in mortality (in patients treated at a general hospital) from 14.5 per cent in 338 cases treated without chemotherapy between 1934 and 1938 to 4.9 per cent in 244 cases treated between 1942 and 1948.

In 1946, Crile[4] recommended the use of large doses of penicillin (100,000 units every three hours) in the treatment of peritonitis of appendiceal origin. He suggested "that the mechanism of action of large doses of penicillin in mixed infections is against the gram-positive cocci. *Escherichia coli* is known to inactivate penicillin, hence large doses of penicillin must be given for long periods of time if effective action against the cocci is to be obtained." With the virulent gram-positive cocci thus controlled, the peritoneum could handle the *Escherichia coli* which were usually of low virulence. Of twenty-one strains of *Escherichia coli* tested by Altemeier[3] three were found to be virulent. In his experience the most effective chemotherapy has been the "combined, parenteral administration of sulfadiazine and penicillin or that of penicillin, sulfadiazine, and streptomycin. When used alone in a high dosage of 100,000 to 500,000 units every two or three hours, penicillin is effective in the great majority of instances, with the exception of those infections caused in part by virulent gram-negative bacteria."

A drug which would be effective against the gram-positive cocci and also the gram-negative bacilli would be the drug of choice in the treatment of peritonitis secondary to rupture of the appendix. Aureomycin, an anti-

* From the Research Foundation of The Children's Hospital of the District of Columbia.

biotic derived from a strain of *Streptomyces aureofaciens*, seemed to be such a drug. It has been found to be effective against a wide range of gram-positive and gram-negative organisms. The drug may be given orally, intramuscularly, and intravenously.

When aureomycin* became available for clinical use at Children's Hospital it was decided to utilize it in the treatment of peritonitis secondary to perforation of the appendix. Recently Wright and his associates[5] have reported a series of fifty-two patients with acute peritonitis treated with aureomycin. Thirty-five of these cases of peritonitis were secondary to ruptured appendix, and six were children between the ages of four to nine years. All six recovered—five uneventfully, and one after a stormy course with development of a wound abscess. These investigators feel that the use of this drug has further reduced the mortality of peritonitis in their hospital.

At our hospital the drug was given to patients who had findings of generalized peritonitis and had not received other antibiotics or sulfonamides. Five patients† who fulfilled these criteria have been treated. Therapy consisted of operation soon after admission, and the administration of aureomycin either orally or intramuscularly. Parenteral fluids were given as indicated in each case.

SUMMARIES OF THE FINDINGS AND COURSE OF THE FIVE PATIENTS TREATED

Case No. 1 O. J. 47-5775

O. J., an eight year old Negro female, was admitted on February 5, 1949, with a history of anorexia for three days. Two days prior to admission she developed fever, vomiting, and abdominal pain. On admission her temperature was 102.0 F., pulse was 120, respirations 20 per minute, and blood pressure 105/60. Examination revealed rigidity and rebound tenderness over the right lower quadrant of the abdomen, tenderness in the right flank, and tenderness over the right costovertebral angle. The white cell count was 20,400 per cubic millimeter with 78 per cent neutrophiles and a shift to the left. Operation was performed six hours after admission. When the peritoneum was opened a small quantity of thin, cloudy fluid which had a fecal odor welled up into the wound. *Pseudomonas aeruginosa* and *Diplococcus pneumoniae* were cultured from this fluid. An inflamed, gangrenous, ruptured appendix was removed with much difficulty. The wound was closed tightly with no drain utilized. Immediately following operation aureomycin was started, 40 milligrams being given intramuscularly every eight hours for two days. Following this she received 500 milligrams orally

* Aureomycin supplied by Lederle Laboratories.

† Four of the five patients were operated upon by the surgical house staff, and the fifth was a patient on the service of Dr. Richard L. Jackson.

every four hours for three days. Although the patient never appeared toxic her temperature remained elevated for nine days after the operation (Figure 1). On the fourth post-operative day she took liquids well, on the sixth day a soft diet, and on the seventh day a regular diet. On the sixth post-operative day the aureomycin was increased to 1,000 milligrams every four hours and this dosage was given for the next three days. On the ninth day after operation a wound abscess ruptured and drained spontaneously.

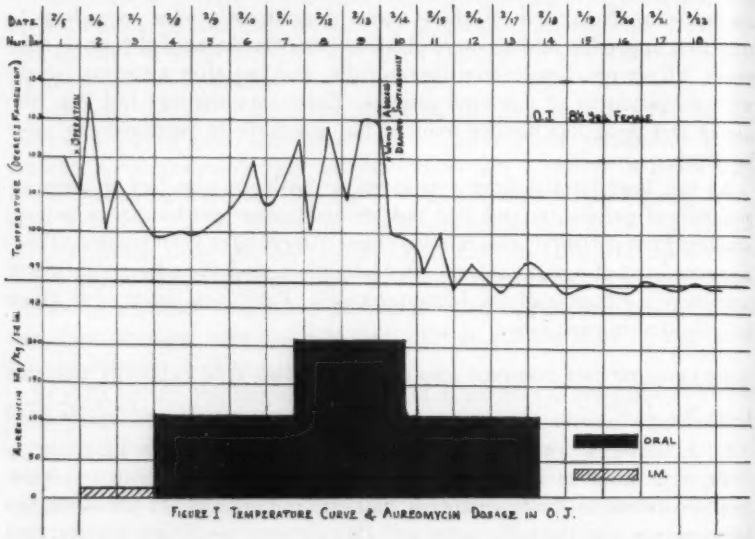

FIGURE 1 TEMPERATURE CURVE & AUREOMYCIN DOSAGE IN O. J.

Escherichia coli and a few colonies of non-hemolytic *Staphylococcus aureus* were cultured from the wound. Six hours later the temperature returned to normal and remained normal, and the patient was walking about the ward with no difficulty. Aureomycin was continued for approximately four more days in a dosage of 500 milligrams every four hours. She was discharged in good condition eighteen days after admission.

Case No. 2 T. H. 49-2598

T. H., a five year old white male, was admitted on February 24, 1949, with a history of fever, vomiting, and epigastric pain of three days' duration. On the day prior to entry he had received castor oil, and on the next day he complained of pain in the right shoulder. His temperature on admission was 102.4 F., his pulse 90 per minute, and respiration 20. Examination revealed his abdomen to be flat but with generalized tenderness and rigidity which was most marked over the right lower quadrant. Urinalysis

was normal. There were 10,000 white blood cells per cubic millimeter with 88 per cent neutrophiles and a marked shift to the left. Operation was performed on the day of admission. On incision of the peritoneum 500 milliliters of thick, foul smelling pus exuded. *Escherichia coli* was cultured from this material. A gangrenous, ruptured appendix was removed from the pelvis. The peritoneum was closed tightly, and a drain was left in the wound down to the peritoneum. Aureomycin was given intramuscularly in a dose of 50 milligrams every six hours for thirty hours and then 250 milli-

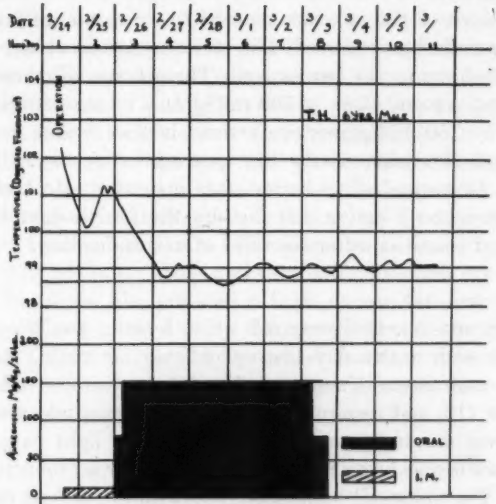

FIGURE 2. TEMPERATURE CURVE & AUREOMYCIN DOSAGE IN T. H.

grams orally for approximately six days. The patient was maintained on parenteral fluids for three days following operation. He took liquids well by the fifth post-operative day and a regular diet by the eighth day. His temperature had returned to normal forty-eight hours after operation and in general he made an uneventful recovery. He was discharged on the twelfth hospital day.

His temperature course is shown in Figure 2 and is in general representative of that of the four patients in whom a drain was left down to the peritoneum.

Case No. 3 W. P. 49-7916

W. P., an eight year old Negro male, was admitted on June 24, 1949, with a two day history of low grade fever, running nose, and intermittent, generalized abdominal pain. He had received castor oil the day before

coming to the hospital. Examination revealed a boy who was lying in bed with his legs doubled up. His temperature was 102.8 F., pulse 120, and respirations 34. Slight, generalized spasm of the abdominal muscles was noted and this was more marked over the lower abdominal area. Peristalsis was normal, and rectal examination was inconclusive. Urinalysis was normal. The white cell count was 15,600 with 79 per cent neutrophiles and a shift to the left. A laparotomy was performed twenty-four hours after his admission. On opening the peritoneum a large quantity of pus was found. *Pseudomonas aeruginosa* and non-hemolytic streptococci were cultured from this pus. As much of the pus was aspirated as possible, and an inflamed perforated appendix was removed. The peritoneum was closed tightly and a drain placed down to the peritoneum. Three hours after operation the patient received an oral dose of 500 milligrams of aureomycin, and this was followed by 250 milligrams every three hours for nine days. He had mild abdominal distension on the first post-operative day. His temperature returned to normal sixty hours after operation. He took fluids by mouth post-operatively and a soft diet by the fourth day. He was discharged in good condition after ten days of hospitalization.

Case No. 4 J. L. 49-7972

J. L., a five and one-half year old white female, was hospitalized on June 25, 1949, with a two day history of fever, anorexia, vomiting, abdominal pain, and urinary frequency. Her temperature on admission was 102.0 F., pulse 110, and respirations 22. Her abdomen was distended and rigid. There was marked generalized tenderness to light palpation. Peristalsis was described as being hypoactive. Except for acetonuria, urinalysis was negative. The white cell count was 8,300 with 77 per cent neutrophiles. Operation was performed six hours after admission. On opening the peritoneum a large quantity of free, purulent fluid was released. Culture of this material revealed *Pseudomonas aeruginosa*. An inflamed, perforated appendix was removed. The peritoneum was closed and a drain placed in the wound down to the peritoneum. Aureomycin was given intramuscularly in a dose of 50 milligrams every six hours for forty-eight hours. Parenteral fluids were also administered for the first forty-eight hours. The patient took some liquids orally on the first post-operative day. Oral aureomycin 250 milligrams every four hours was started after forty-eight hours and a regular diet on the fifth day. On the ninth day she had mild vomiting which ceased when the aureomycin was discontinued. She was discharged in good condition on the eleventh hospital day.

Case No. 5 B. F. 47-817

B. F., a four year old Negro female, was admitted on June 20, 1949. She had been hospitalized one month prior to this admission because of

abdominal pain but physical findings were equivocal at that time. Ten days before the present admission she had vomited twice but had no other complaints. Four days prior to entry she had abdominal pain which disappeared and recurred on the day of admission. On examination it was noted that she kept her knees flexed. Her temperature was 101.6 F., pulse 64, and respirations 20. The abdomen was flat but spasm and tenderness were present in both lower quadrants being more marked on the right side. A profuse, foul smelling vaginal discharge was present but no pathogens could be cultured. Urinalysis revealed acetonuria and clumps of pus cells. The white cell count was 12,000 per cubic millimeter with 83 per cent neutrophiles and a shift to the left. Five hours after admission a laparotomy was performed. The cecum was adherent and there was a large amount of edema and fibrin around it. A large amount of foul smelling pus was found. *Escherichia coli* and a few colonies of non-hemolytic streptococci were cultured from the pus. The appendix was located retrocecally and was bound down to the lateral abdominal wall. The appendix was removed, the peritoneum closed tightly, and a drain inserted down to the peritoneum. For the first twenty-four hours 100 milligrams of aureomycin was given intramuscularly every six hours and then 250 milligrams orally every three hours for four days. She vomited a little during the first post-operative day but was taking a soft diet by the second day. Her temperature came down to 100.4 F. in forty-eight hours and remained normal after ninety-six hours. Her course was otherwise uneventful and she was discharged after seventeen hospital days.

DISCUSSION

While the number of patients reported here is small, it is felt that their presentation would be worthwhile in view of the fact that aureomycin was the sole drug utilized and the response was encouraging. Some pertinent data on these five patients are summarized in Table I.

The duration of illness prior to operation in these children varied from two to four days with an average of three days. Their ages ranged from four to eight and one-half years. The peritonitis was considered to be generalized in all five patients. Two had received castor oil prior to admission.

At the time of operation the appendix was removed and the peritoneum was closed tightly in all patients, but in four a drain was inserted down to the peritoneum. It is interesting to note that of these five patients the one whose wound was not drained remained febrile for the longest time (eight days as compared to from two to four days for the others). However, even this child showed no signs of toxicity.

In this group of patients the drug was given intramuscularly or orally. No attempt was made to calculate a precise dose on a weight basis. The

TABLE I

Summary of Five Cases of Peritonitis Treated with Aureomycin

PATIENT			DURATION OF ILLNESS UNTIL OPERATION	OPERATIVE FINDINGS*	MAXIMUM WHITE CELL COUNT	CULTURE OF PERITONEAL FLUID	AUREOMYCIN THERAPY			RESULTS
Initial	Age	Sex					Dose	Days	Total Dose	
	yrs.		*days*				*Mgm/Kgm/24 hrs.*		*Gms.*	
1. O. J.	8½	F	3	Free cloudy fluid with fecal odor; appendix retrocecal; wound closed tightly.	20,400	*Pseudomonas aeruginosa; Diplococcus pneumoniae*	I. M. 4.1 Oral 104 Oral 207 Oral 104	2 3⅔ 3 3⅔	40.24	Afebrile in eight days; wound abscess; recovery otherwise uneventful.
2. T. H.	6	M	3	Large amount of thick, foul smelling pus; peritoneum closed; wound drained.	10,000	*Escherichia coli.*	I. M. 10.0 Oral 150	1¼ 6	16.75	Afebrile in forty-eight hours. Recovery uneventful.
3. W. P.	8½	M	3	Large amount of pus; peritoneum closed; wound drained.	18,900	*Pseudomas aeruginosa;* non-hemolytic streptococcus.	Oral 91	9	18.75	Afebrile in sixty hours. Recovery uneventful.
4. J. L.	5½	F	2	Large amount of free purulent fluid; peritoneum closed; wound drained.	8,300	*Pseudomonas aeriginosa*	I. M. 11 Oral 84	2 6½	9.15	Afebrile in sixty hours. Recovery uneventful.
5. B. F.	4	F	4	Cecum adherent; large amount of foul smelling pus; appendix retrocecal and bound down to lateral abdominal wall; peritoneum closed; wound drained.	12,000	*Escherichia coli;* non-hemolytic streptococcus	I. M. 23.5 Oral 118	1 4	8.40	Afebrile in ninety-six hours. Recovery uneventful.

* A ruptured appendix was removed in each case.

intramuscular dose used in four of the five patients treated varied from 4.1 to 23.5 milligrams per kilogram of body weight for twenty-four hours, with an average of 12.1 milligrams. The oral dose for the five patients varied from 84 to 207 milligrams per kilogram for twenty-four hours with an average of 126 milligrams. The total dose varied from 8.4 grams to 40.2 grams with the average being 18.6 grams. However, the average total dose for the four patients whose wounds were drained was 13.3 grams. One patient showed mild vomiting on the eighth day of therapy which may have been due to the medication.

Intramuscular administration may be accompanied by local pain, induration, and tenderness. In addition, it has been our impression in treating other conditions that the results from oral and intravenous administration are better than those obtained via the intramuscular route. Since the drug can be administered intravenously, perhaps the most advantageous form of therapy may prove to be the giving of aureomycin intravenously until the patient is able to tolerate the drug orally. Nausea, vomiting, and diarrhea are possible side effects of aureomycin when given orally, and this may be an added reason for intravenous administration for one to three days post-operatively.

Although the number of patients treated here is too small to justify any definite conclusions, we feel that the results are gratifying and that further investigation is warranted.

SUMMARY

1. The use of aureomycin in the treatment of five cases of peritonitis secondary to rupture of an inflamed appendix is reported.
2. Operation was performed in each case followed by the administration of aureomycin.
3. Removal of the appendix and tight closure of the peritoneum with drainage of the wound seems to be the operation of choice.
4. The results were considered good in the five patients treated.

ADDENDUM

One more patient has been treated since this paper was written. She was a five and one-half year old white female who had a ruptured appendix and free pus in the peritoneal cavity from which *Escherichia coli* was cultured. She received 40 milligrams per kilogram of aureomycin intravenously every twenty-four hours for two days followed by 75 milligrams per kilogram orally every twenty-four hours for four days. Her total dose was 7.9 grams. Her abdomen was soft in forty-eight hours. She took liquids well post-operatively, a soft diet on the fourth post-operative day, and a regular diet by the fifth day. She was discharged in good condition six days after her operation.

* A ruptured appendix was removed in each case.

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THE GUILLAIN-BARRÉ SYNDROME

Case Report No. 180

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Paul Kaufman, M.D.

48-11371

D. C., a four year old white male*, was admitted to The Children's Hospital on October 1, 1948 with the chief complaint of "staggering gait" of three days' duration.

The present illness had its onset three weeks prior to hospitalization at which time the patient complained of paresthesias in both lower extremities after having been seated for a long period of time. The parents attributed this condition to pressure. For the next two weeks the patient complained of intermittent paresthesias of both the upper and lower extremities. Most frequently these complaints were referred to the lower extremities. Five days before admission, running nose, cough, and a slight fever became manifest, these symptoms persisted for two days. At this time an ataxic gait was noted and, in addition to the parasthesias, pain was present in the lower extremities. Forty-eight hours prior to admission, the patient refused to support his own weight, and this persisted until hospitalization.

The past and family history were entirely non-contributory. There were no recent illnesses, inoculations, or vaccination. No contact history with any of the infectious diseases could be elicited. There had been no ingestion of any noxious agents. Milk and water supply could not be indicted as etiologic agents. Familial neurological disorders were denied. The feeding and developmental progress were normal.

The physical examination on admission revealed a temperature of 98.6 F., pulse rate of 86 per minute, and respirations of 20 per minute. The patient was a well developed and nourished, alert white male who was cooperative throughout the examination. There was a generalized shotty, non-tender lymphadenopathy noted. Slight resistance of the neck and back to full flexion was present. The pupils were equal and reacted to light and accommodation. Fundoscopic examination disclosed no abnormalities. The pharynx was somewhat injected. The respiratory rate was regular and chest expansions were equal bilaterally. No weakness of the intercostal muscles or the diaphragm was present. All the superficial reflexes were normal while the deep tendon reflexes were absent. The Brudzinski and Kernig tests were positive. The cranial nerves were intact. No definite muscular weakness was present although this was difficult to evaluate because of the pain produced by motion. A marked ataxia was noted: the finger-to-nose

* Private patient of Richard H. Todd, M. D.

and heel-to-knee tests could not be performed; the patient walked on a wide base with his arms fixed.

The laboratory investigation was extensive. The admission hemogram revealed 13.0 grams of hemoglobin; 5,200,000 erythrocytes, and a leukocytosis of 11,300 with a differential of 72 per cent neutrophiles, 1 per cent basophiles, 26 per cent lymphocytes, and 1 per cent monocytes. Repeated hemograms throughout hospitalization showed essentially no change except for an increasing eosinophilia which on discharge ranged as high as 24 per cent of the total leukocyte count. Urinanalyses were entirely normal. The tuberculin skin test was negative. On repeated examinations, the erythrocyte sedimentation rate (Wintrobe-Landsberg) was 14 millimeters per hour. The blood calcium was 13 milligrams per cent and serum phosphorus 1 milligram per cent. Serologic test for syphilis failed to reveal any abnormality. No basophilic stippling of the erythrocytes was seen on examination of the peripheral blood smear. X-ray examination of the skull and long bones was normal. An electroencephalogram showed evidence of slight irritation but no gross abnormality. The examinations of the spinal fluid obtained from lumbar puncture were of interest. The hydrodynamics were normal. Two examinations were entirely normal; whereas a third examination showed an albumino-cytologic dissociation, the protein content having risen to 100 milligrams per cent. Culture of these specimens grew no organisms. The Wassermann, Kahn and colloidal gold examinations were within normal limits.

During hospitalization the patient received only palliative therapy. At no time was his temperature elevated. The only significant features noted were an increase in the ataxia, the absence of any marked paralyses, the persistence of parethesia and pain with no alteration of the abnormal neurological findings present on admission.

The patient was discharged on October 14, 1948, fourteen days after admission. The progress at home under the guidance of a private physician was one of gradual and complete recovery. At no time were any paralyses or muscular weaknesses present. The pains and paresthesias gradually diminished until two months after discharge when they had disappeared entirely. He was afebrile except during episodes of rubeola closely followed by rubella.

Four months from the onset of his illness he was not only asymptomatic but also free from any abnormal physical findings, and has remained in this state of well-being until the present time, fourteen months after discharge.

DISCUSSION

In 1916 Guillain, Barré and Strohl described a syndrome in which there is slowly progressing ascending paralysis of the body starting in the lower

extremities and which is characterized by albumino-cytologic dissociation of the cerebro-spinal fluid, and a favorable prognosis.

Numerous cases of neuritides have been reported since then and although they do not possess all the characteristics of the originally described syndrome, they closely resemble it. Among these related syndromes the following have been included: acute infective polyneuritis, acute febrile polyneuritis of unknown origin, acute neuronitis, acute benign infectious myelitis, acute infective meningomyeloneuritis, polyneuritis with facial diplegia, myeloradiculitis, infective neuronitis, and radiculoneuritis. Because of the close relationship, it is probable that these syndromes represent various degrees of severity of the same disease process.

Until recent times it has been supposed that this disease complex occurred only in the older age groups. However, numerous cases in childhood are now being reported in the literature[1, 2, 3, 4, 5, 6].

Although the etiology of this syndrome is not known, and the pathological lesions are not characteristic, the clinical picture is well defined. Generally there is a history of a slight upper respiratory system infection eight to ten days prior to the onset of specific neurologic symptoms. This condition occurs mainly in persons between the ages of twenty to fifty years and only occasionally in the younger and older age groups. Shortly after the onset of catarrhal symptoms, characteristic peripheral neuritis makes its appearance. It develops symmetrically in the lower extremities. Concomitant muscular tenderness and sensory changes may be present. Many patients later develop a symmetrical flaccid paralysis of the lower extremities. In some the paralysis continues to advance upward with the subsequent production of a quadriplegia. Atrophy of these involved muscles does not occur. The rate of spread as well as the degree of involvement is quite variable. The paresis may be manifested only by awkwardness in the voluntary movements (ataxia) while in others it may be complete. It should be noted that sensory changes may be the initial complaints and when present, they are generally limited to the distal portions of the extremities. Cranial nerve involvement particularly of the seventh (facial) with a resultant diplegia occurs frequently.[10] Characteristically the paresis, paresthesias, and muscle tenderness affect first the lower extremities and then the upper with rare involvement of the respiratory muscles. The onset and course are usually afebrile when other secondary infections are absent. The deep reflexes are abolished or markedly dimished but the superficial reflexes are present. There are few changes in the electrical reactions of the muscles and nerves, and slight change in objective sensibility. Occasionally there are disturbances in sphincter control.

The cerebro-spinal fluid shows a constant and marked increase in protein although it is not high early in the disease. There is no pleocytosis; Guillain used the term albumino-cytologic dissociation to designate these

findings. Xanthochromia may be present; the Wassermann reaction of the spinal fluid is negative. Slight precipitation may be present in the middle and end zones of the colloidal gold curve.

The mental condition of the patient is unaltered and the prognosis is favorable with gradual recovery taking place over a period of weeks or months, and there are usually no sequellae. Complete recovery is to be expected in four to six months. It must be stressed that a fatal outcome, while not common, does occur.[7, 8, 9, 10] Death seems to occur most commonly in those cases in which there is a paralysis of the respiratory muscles.

Little pathologic material has been obtained owing to the favorable outcome. In the cases that have been reported, in which post-mortem studies have been made, diffuse involvement of the nervous system was found, with the most marked changes in the spinal roots and peripheral nerves, less marked changes in the meninges, and degenerative changes and hyperemia of the grey matter of the cord.[1] Sections from the spinal nerve roots show marked congestion and edema of the nerve fasciculi. There is cellular infiltration of the anterior nerve roots at all levels, and marked distortion of the axis cylinders is present. The myelin sheaths are swollen and disrupted.[7]

The Guillain-Barré syndrome may simulate many other diseases.[11, 12] Negative smears and cultures for the Klebs-Loeffler organism together with the absence of cervical adenitis rule out diphtheritic neuritis. Encephalitis must be considered in those cases in which there is cranial nerve paralysis. However, the absence of personality changes and the spinal fluid findings make the differentiation conclusive. Botulism may be excluded by a consideration of recent food ingestion, together with the absence of abdominal complaints and favorable outcome in infectious polyneuritis. Acute anterior poliomyelitis often causes confusion in the differential diagnosis. In poliomyelitis the paralysis is usually not progressive and paresthesias are absent. The course of the disease is a febrile one, and paralytic residua with atrophic changes are common. Berand[6] has stressed the diagnostic value of electro-diagnosis in the early differentiation of the meningoradicular syndromes of the Guillain-Barré type. The essential point is the early and total loss of faradic excitability of the nerve and muscle in poliomyelitis. In addition hypercytosis parallels albuminosis in the spinal fluid. Serologic tests together with the spinal fluid reactions are sufficient to establish or rule out the diagnosis of syphilis. The neuritis accompanying diabetes mellitus disappears when the diabetes is controlled. Finally in the polyneuritis associated with plumbism there is a history of exposure to lead together with gingivitis, wrist-drop, basophilic stippling of the erythrocytes, and characteristic radiographic changes in the long bones.

At the present time there are no specific therapeutic measures in the management of infectious polyneuritis. Radiation therapy has been recommended by some investigators. Beneficial effects are believed to accompany this measure.[13] Other therapeutic regimes include the use of prostigmine injections together with local hot-pack applications.[3] Any plan of therapy should have as its aim the prevention of muscular deterioration.[14] Treatment should consist of bed rest, physiotherapy from the onset of motor weakness, and a high vitamin diet (particularly thiamin-hydrochloride). Activity is graded and permitted to the extent of the patient's capability.

SUMMARY

1. A case of probable Guillain-Barré syndrome with favorable outcome has been presented.

2. A detailed discussion of this disease together with a differential diagnosis and recommended therapeutic regime has been given.

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ERYTHEMA MULTIFORME ASSOCIATED WITH BACILLARY DYSENTERY

Case Report No. 181

Charles L. Waite, M.D. J. Y. 49-1283

A twelve months old white male was admitted on September 19 because of fever, diarrhea, and a rash. Five days prior to admission he developed a rash on his arms, legs, and trunk and shortly after he developed loose, watery, green stools. He had six to ten bowel movements a day. There was no blood or mucous in the stool and the odor was not abnormal. The following day he developed a fever of 102.0 F. There was no associated vomiting, loss of appetite, or cough. The formula was made with unboiled well water. The well had not been inspected or certified for at least two years at the time of admission.

Past history included one previous episode of diarrhea associated with an upper respiratory infection at the age of eight months. This cleared up promptly in three days with symptomatic and supportive treatment.

The family history showed three older siblings, all with one or more allergic manifestations in their medical background, but none of whom had diarrhea or any illness at the time of the patient's admission.

Physical examination revealed a well developed, well nourished white male with a low grade fever (100.5 F., rectally), in no acute distress, but showing signs of moderate dehydration. The most remarkable thing on examination was the rash which covered the extremities and the entire chest and abdomen. There was no rash on the scalp, palms, or soles.

The rash varied from a pink flush to a deep red hue and was macular, papular, vesicular and urticarial in nature and showed many forms; irregular, oval, annular, crescentic and punctate. There evidently was no severe pruritus associated with it as the patient did not scratch the lesions. There were no conjunctival or buccal mucous membrane lesions. The remainder of the physical examination was negative.

Antihistamine therapy in the form of Elixir of Pyribenzamine drams one every four hours was started. The blood count on admission showed a 4 per cent eosinophilia. By the following day, August 20, the rash was beginning to fade and new lesions had appeared. The diarrhea persisted and the patient was hydrated using intravenous and hypodermoclyses. The stool cultures taken on September 19 and 20 were reported as positive for Shigella sonnei and treatment with aureomycin hydrochloride, 250 mgms. every four hours, was begun. The following day, as the rash had now disappeared, the antihistamine was discontinued.

The general clinical improvement of the patient was marked and the stool cultures taken on September 21 and the succeeding days were all negative. The white count and differential of September 26 showed 12 per cent eosinophilia. On September 27, as the patient was about to be discharged, the rash reappeared and his temperature rose to 100.8 F. The

FIG. 1. J. Y. Close-up of rash taken early during its recurrence showing the different types of lesions.

rash was almost identical with that present on admission and rapidly became full blown.

Photographs were taken (Figure 1.) and treatment with an antihistamine was reinstituted. The rash again faded rapidly, the patient was discharged and sent home on a daily dose of antihistamine. The mother reported later that the rash did not recurr.

DISCUSSION

Erythema multiforme may occur as a separate disease entity or accompany a certain specific disease, as in the case reported. The true etiology of erythema multiforme is unknown. Anderson[1] believes that the probable pathogenesis is a sensitization in the small cutaneous blood vessels of certain individuals to any one of many allergenic or toxic substances. In this case the toxin of Shigella sonnei may well have been the allergen. The marked response to antihistaminic therapy also points to an allergic reaction as the probable cause. Typhoid fever and diphtheria, both of which produce an exotoxin, are occasionally accompanied by erythema multiforme. The eruption has also been reported following the ingestion of certain foods and the administration of some drugs. Dilantin, barbiturates, and sulfonamides are among the known offenders.[2] Foci of infection in the teeth, tonsils, sinuses, and genito-urinary tract and certain chronic visceral diseases may also be responsible.[3]

As the name "multiforme" implies the lesions may be macular, papular, urticarial, circinate, vesicular, or bullous. Occasionally as in the case here considered the lesions will be of several different forms, but usually one type predominates in a given case.

There is a tendency to recurrence and a seasonal incidence has been noted in those cases occurring as a disease entity. Pruritis is not usually present unless some of the lesions are urticarial. The eruption's appearance may be accompanied by a low grade fever as was noted in the recurrence in this case.

Erythema multiforme is almost always a self-limited disease and its occurrence during the course of another disease is not a serious complication. Therapy with antihistaminics may prove to be effective.

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M. L. O. a six year old white female, was admitted for the first time on September 28, 1944, with the following past history. Five weeks before admission pains were noted in the stomach and in the hip. In duration, the pains lasted one day and recurred about three times weekly until admission. A diagnosis of "worms" was made but the instructions for gentian violet were not followed because the child went to West Virginia. On arrival the left hand and both knees became swollen and painful and at the same time "red, elevated lumps and blisters" appeared on the arms and legs together with a recurrence of abdominal and hip pains. No elevation of temperature was present during this and subsequent attacks. An unknown medication was used and the attack cleared on the following day; however, all other attacks cleared spontaneously within the same time. During this visit to West Virginia, the patient drank city water and raw cows' milk. The picture remained unchanged except for weight loss of four and one-half pounds and increasing pallor in the presence of a good appetite. One stool specimen was noted to contain a worm-like object two inches in length.

The family, social, past medical, and immunization histories are all non-contributory except that a twin sibling died of bronchopneumonia at six and one-half months.

On admission a chronically ill, poorly nourished, rather pale white female was seen who weighed thirty-nine pounds and was afebrile. The height was 47 inches. Cervical lymphadenopathy was minimal. The liver, spleen, and kidneys were not palpable and the remainder of the physical examination was negative except for an erythematous maculo-papular non-confluent rash on the dorsi-lateral aspect of both thighs and both forearms. Intermittently on following examinations, there was subjective periumbilical pain and objective flank tenderness. The temperature remained flat during the entire admission. The blood pressure averaged 110/80 but varied between 140 systolic and 68 diastolic. The pulse averaged 100. One examiner thought the liver was enlarged 3 centimeters below the right costal margin. Periodically during the admission the rash would return and was described by many observers as purpura.

The following studies were within normal limits or were negative: vaginal smear; febrile antigens; stool ova and parasites; stool occult

blood; serology; electrocardiogram; chest x-ray; non-protein nitrogen; intravenous urogram; ultraviolet skin irradiation; a skeletal muscle biopsy; O.T.; and a Schick test.

A sedimentation rate on admission was 24.5 millimeters per hour, but later fell to 17 millimeters per hour.

Daily urinalyses over the one month period of admission disclosed the following observations in common on all specimens: turbid, acid, 1.010–1.025 specific gravity, sugar and acetone negative, 20–2000 milligrams per cent albumen, numerous erythrocytes and leukocytes, hyaline and granular casts.

The bleeding time was one minute or less (two occasions) and the coagulation time was three minutes. The thrombocytes varried from 125,000 to 280,000 per cubic millimeter. The prothrombin time was normal.

Hemograms varied as follows: 12–13 grams of hemoglobin, 3.1–4.4 million erythrocytes, 11.2–22.6 thousand leukocytes of which 63–78 per cent were segmented and 19–35 per cent were lymphocytes. Small transfusions were given periodically.

At the time of discharge on November 25, the condition was unchanged except that the weight was 43 pounds. By January the condition was still the same but the weight was 46 pounds and the height was 46 inches.

She was again admitted in May 1945, and the above state had persisted during the interim with only one bout of purpura in December. A repeat vaginal smear was negative, a hemogram showed 13.0 thousand leukocytes with 75 per cent segmented and the urinalyses were unchanged. The blood pressure was 120/90 on one occasion but averaged 110/70 during the eight days of admission.

In June of the same year, the last time the child was seen, the mother stated that the urine was clear. Two infected teeth were extracted at that time uneventfully and it was noted that the tonsils were cryptic and a tonsilectomy was advised.

The mother stated over the phone in January 1950 that the child was normal in every way and had been asymptomatic since last seen in 1945.

DISCUSSION

John E. Cassidy, M. D.: We have here a six year old white female who on admission presented the following significant features: recurrent attacks of abdominal pain and pain in one hip lasting about twenty-four hours and occurring about three times a week for the preceding five weeks; the possible presence of a worm infestation which was untreated; associated with one of the attacks of abdominal pain, there occurred skin involvement of the arms and legs described as "red, elevated lumps and blisters;" the absence of fever; weight loss of four and one-half pounds; increasing pallor; and history of ingesting raw milk while on a trip to West Virginia. The physical examination revealed malnutrition and an erythematous maculopapular

non-confluent rash on the dorsi-lateral aspect of both thighs and forearms This rash was transient in character and described by many as purpura.

With this information there are various conditions to be thought of, many of which can be eliminated before considering the laboratory studies.

We are told that the patient had worms and must assume that this was established by obtaining stool specimens and indentifying the ova. The significance or lack of significance of this will be discussed later.

Rheumatic fever should be considered but can be quickly dismissed because of the absence of fever and migratory arthritis. Lupus erythematosis disseminata must also be considered but there too the absence of fever and the characteristics of the joint pains would be against this. The skin manifestations in lupus may resemble those which this patient exhibited. Exposure to sunlight is apt to cause an exacerbation of these. Brucellosis must be considered but here again absence of fever is strongly against this. Libman Sachs syndrome, which resembles lupus except that in addition there is renal and endocardial involvement and periarteritis nodosa must be mentioned.

Because of the characteristics of the rash, which varied at first and then became purpuric, there is a large group of conditions to be thought about and these identifications will depend a great deal on the laboratory findings. This group is the purpuras. An outline or classification of these can be given as follows:

I. Thrombocytopenic
  A. Primary or idiopathic
  B. Secondary
    1. Chemical agents
    2. X-rays and radium
    3. Blood disorders
      a. Leukemia
      b. Aplastic anemia
      c. Hypersplenism
    4. Infections

II. Non-thrombocytopenic
  A. Anaphalactoid
    1. Henocks
    2. Schonleins
  C. Embolic
  D. Chronic disease
  E. Avitaminosis
  F. Miscellaneous
    1. Mechanical
    2. Orthostatic

With these above conditions in mind we can consider the laboratory studies and results which are presented.

The hemogram showed a variable and slight anemia, normal thrombocyte count, and a leukocytosis. Bleeding, clotting time, and prothrombin levels were normal. The only other positive laboratory findings were in the urine i.e., the constant presence of albumin, red and white blood cells and casts. Bone marrow aspiration and study might have been enlightening but in view of the subsequent course of the patient, leukemia is certainly ruled out.

If we consider the involvement of the skin as essentially or mainly purpuric in nature then we must consider more strongly the non-thrombocytopenic purpuras and specifically the anaphylactoid group. The anaphylactoid purpuras are those non-thrombocytopenic purpuras characterized by the presence of one or more of the common manifestations of allergy i.e., erythema, urticaria, effusions of serum into subcutaneous or submucous tissues or viscera. The purpura itself may be simple or associated with vesicle formation or even at times bullae and necrosis of tissue.

Our patient fits into this category very nicely. The urinary findings must be explained either on the basis of a nephritis or allergic changes, so called, in the renal parenchyma similar to those which occurred in the skin and subcutaneous tissues. This is a rather unusual type of involvement but it can occur, and I believe it must be considered as part of the generalized allergic state.

The presence of a worm infestation was not established or we might consider this as the trigger mechanism for the whole picture.

The course of this patient, similar recurrent attacks for almost a year with clearing of the urine, and regain in weight all tend to rule out the other diseases mentioned and leave us with the diagnosis of anaphylactoid purpura. At times this can be further broken down depending on whether the abdomen or joints are mainly involved into Schonleins and Henochs but more often there is a blending or overlapping so that the first term is a more suitable one.

PATHOLOGIC DISCUSSION

F. R. Leyva, M.D.: I saw this patient on her various visits to the hospital and later in the clinic. We asked her to come in yesterday in order to report her present condition at this conference. She is now twelve years of age and has been in excellent health for at least two years. Her weight and height and blood pressure were quite normal and there were no abnormal physical findings. A brief laboratory survey showed the urinalysis, non-protein nitrogen, and serum proteins to be within normal limits. We

agree with Dr. Cassidy that this represents one of the anaphylactoid purpuras, probably the Henoch type because of the prominence of abdominal pain. The intensity and persistence of the urinary findings in this patient are unusual features if this is truly an anaphylactoid purpura. However, one may wonder whether this child may not have had a benign glomerulonephritis in addition to her purpura.